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KATHRYN M BROWN
MORGAN AND FINNEGAN
345 PARK AVENUE
NEW YORK NY 10154

EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1806	15

DATE MAILED: 11/13/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 9/11/95 6/10/96 ☐ This action is made fin

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-94
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-5, 7, 8, 10-16, 18-39 are pending in the applicatio
   Of the above, claims _____ are withdrawn from consideration.
2. ☑ Claims 6, 9, 17 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-4, 8, 10-16, 18-39 are rejected.
5. ☑ Claims 5, 7 are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

DETAILED ACTION

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1806.

2. Applicant's Application Status Inquiry, filed 6/10/96 (Paper No. 14), is acknowledged. The instant Office Action will serve as a response to this inquiry.

3. Applicant's amendment, filed 9/11/96 (Paper No. 13), is acknowledged.
Claims 6, 9 and 17 are canceled.
Claims 3, 10, 24, 25, 26, 28, 30-32 have been amended.
Claims 35-39 have been added.

Claims 1-5, 7, 8, 10-16 and 18-39 are pending and being acted upon presently.

4. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 9/11/96 (Paper No. 13). The rejections of record can be found in the previous Office Action (Paper No. 12).

5. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 8.

Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes (see 7. Views).

Applicant will submit formal drawings when allowable subject matter is indicated.

6. Upon reconsideration of the art in conjunction with applicant's amendment and citations, filed 9/11/96 (Paper No. 13) in conjunction with the Steinberg Declaration under 37 C.F.R. § 1.132, filed 11/29/94; the previous rejections under 35 U.S.C. § 112, first paragraph have been withdrawn.

7. The previous rejection of claims 30-31 under 35 U.S.C. § 112, second paragraph, have been obviated by amending the claims.

8. 27. Claims 1-~~5~~ 4, ~~7~~, 8, 10-16 and 18-39 are rejected under 35 U.S.C. § 103 as being unpatentable over Lasky et al. (U.S. Patent No. 5,098,833; 1449) and Bevilacqua et al. (U.S. Patent No. 5,081,034; 1449) in view of Watson et al. (Nature, 1991; 1449, #23), Kishimoto et al. (PNAS, 1990; 1449, #38;), Kishimoto et al. (Blood, 1991; 1449, #31), Picker et al. (Cell, 1991; 1449, #6) and , The instant claims are drawn to antibodies that recognize a common E-/L-selectin epitope and their use in diagnosis and therapy as well as methods of making said antibodies.

Lasky et al. teach the cloning of L-selectin and its use in the diagnosis and treatment of inflammatory diseases (see entire document). Similarly, Bevilacqua et al. teach the cloning E-selectin and its use in the diagnosis and treatment of inflammatory diseases. As disclosed in the specification, the prior art is replete of examples of L-selectin and E-selectin antibodies which inhibit various models of inflammatory diseases (see pages 1-10 of the specification). Both references teach making selectin-specific antibodies. These references differ from the instant claims by not reciting the particular specificity for antibodies that bind both L- and E-selectin.

Watson et al. teach the use of L-selectin-specific molecules as therapeutic agents to inhibit viral infection or immune function (see entire document). Furthermore, Watson et al. teach that combinations of adhesion molecules may be required to inhibit acute or chronic inflammatory responses (see page 166, column 2, paragraph 3). Here, Watson et al. corresponds the inhibitory effects of the L-selectin chimeric protein and E-selectin expression. Watson teaches that the rational design of anti-inflammatory regents should be based on competitive blocking of leukocyte-endothelial cell interactions.

Kishimoto et al. (PNAS) teach the derivation of a number of L-selectin-specific antibodies including the DREG-56 antibody (see entire document). Kishimoto et al. teach the ability of the DREG-56 antibody to inhibit lymphocyte-endothelial binding in vitro. Kishimoto et al. also compare these observations with the ability of other L-selectin-specific antibodies to inhibit neutrophils and monocytes in addition to lymphocytes, which are useful for treating inflammation in vivo.

Kishimoto et al. (Blood) teach that certain anti-E- and L-selectin antibodies are not additive in their blocking effects on neutrophil-activated endothelial cell adhesion, indicated that these two selectins participate in the same adhesion pathway (see entire document). Also, neutrophil binding to E-selectin cDNA transfect L cells was blocked by anti-L-selectin monoclonal antibody treatment.
Picker et al. teach L-selectin on neutrophils is decorated by sLex carbohydrates and may preferentially present these structures to E-selectin and that the selectins are structurally similar (see entire document).

Therefore, Kishimoto et al. (Blood) and Picker et al. teach the commonality between blocking L- and E-selectin mediated events with the same anti-adhesion antibodies. Therefore, it would have been expected that the ordinary artisan could generate antibodies that bind common epitopes on L- and E-selectin and that such antibodies could inhibit L- and E-selectin mediated events.

Antibodies directed towards a common E-/L-selectin epitope including the use of selectin expressing recombinant cells as immunogen would have expected in view of the above teachings, particularly Kishimoto et al. (Blood) and Picker. Such specificity would have been selected for by routine screening of L- or E-selectin-specific antibodies that inhibited leukocyte-endothelial interactions and their use as diagnostic and therapeutic agents for human inflammatory diseases, as taught by Lasky, Bevilacqua and Kishimoto et al. (PNAS). The claimed limitations of antibodies specific for (common) E-/L-selectin epitopes would have been met by the selection process disclosed in the prior art. The claimed limitations of inhibiting adhesion, leukocyte rolling, tissue damage, and inflammation would have been met by the selection for treating inflammatory diseases, as disclosed in the prior art.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of L-selectin-specific antibodies as therapeutic and diagnostic reagents in treating human inflammatory diseases. The derivation of those antibodies which bind a common E-/L-selectin would have been a result of selecting for these properties. Furthermore, the ordinary artisan would have coordinated addressing multiple adhesion molecules in the rational design of anti-inflammatory reagents including the relationship of E-selectin and L-selectin in leukocyte-endothelial interactions. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Upon reconsideration of the art in conjunction with applicant's amendment and citation, filed 9/11/96 (Paper No. 13) in conjunction with the Jutila and Kishimoto Declarations under 37 C.F.R. § 1.132, filed 9/11/96 (Paper No. 13); the previous rejections under 35 U.S.C. § 103 have been withdrawn with respect to the EL-246 antibody. Therefore, claims 5 and 7 are free of the prior art.

Applicant's amendment, filed 9/11/96 (Paper No. 13), in conjunction with the Kishimoto and Jutila Declarations under 37 C.F.R. § 1.132, filed 9/11/96 (Paper No. 13); but have not been found convincing for the instant claims as currently recited.

It is noted that the instant claims are drawn to antibodies that bind a common epitope on L- and E-selectin. Applicant is invited to bring in the features of the instant EL-246 antibody into the claimed recitation to obviate the prior art. For example, applicant should claim the biological or functional equivalents of the instant EL-246 antibodies with the properties of said EL-2465 antibody including the following properties: antibodies that bind a common epitope on L- and E-selectin, that bind the SCR domain, that block both L- and E-selectin-mediated adhesion such as inhibiting neutrophil binding to cell expressing E-selectin and neutrophil rolling on endothelial cell layers expressing E-selectin and binds selectin from a variety of different animals. As Kishimoto's declaration point out, if antibodies of the present invention do not bind the soluble form of L-selectin, this would be an important limitation to the claimed recitation, if it is supported by the instant specification as filed.

If applicant concurs with the instant suggestions by the examiner, applicant is invited to cancel all pending claims and add new claims that clearly distinguish the features of the instant L-/E-selectin antibodies for clarity. Applicant is reminded not to amend the claims to add new matter.

In view of the newly added references of Kishimoto et al. (Blood, 1991; 1449, #31), Picker et al. (Cell, 1991; 1449, #6) in the rejection under 35 U.S.C. § 103; the expected success of generating antibodies that bind a common epitope between L- and E-selectin. Therefore, applicant's amendment and citation, filed 9/11/96 (Paper No. 13) in conjunction with the Jutila and Kishimoto Declarations under 37 C.F.R. § 1.132, have been fully considered but are not found convincing in that they do not address the newly added references (versus the DREG series of antibodies) and more importantly are directed towards the features of the instant EL-246 antibody, not of all which are recited in the instant claims. Such features would be considered free of the prior art.

For example, the Jutila and Kishimoto declarations point out that the immunogen method of immunization and initial screening procedures and resulting antibodies of the present invention are different from those of Kishimoto (PNAS) and of critical importance the antibodies of the instant invention do not react with the shed L-selectin immunogen taught by Kishimoto (PNAS). Also, both the Jutila and Kishimoto declarations failed to produce antibodies of present invention using the immunogen, method of immunization and initial screening as taught by Kishimoto (PNAS). Applicant argues the clear difference between the DREG-56 antibody and the instant antibodies. Applicant should limit claims to the common E-/L-specific antigenic determinant defined by the EL-246 antibody.

Applicant's arguments are not found persuasive for the claims as currently recited and in view of the New Grounds of Rejection.

10. No claim is allowed.

11. Claims 5 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-7939.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee can be reached on (703) 308-2731. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

LILA FEISEE
PRIMARY EXAMINER
GROUP 1800

Phillip Gambel, Ph.D.
Patent Examiner
Group 1800
November 10, 1996

Phillip Gambel